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RESEARCH ARTICLE

Nerve autografts and tissue-engineered materials for the repair of peripheral nerve injuries: a 5-year bibliometric analysis

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Abstract
With advances in biomedical methods, tissue-engineered materials have developed rapidly as an alternative to nerve autografts for the repair of peripheral nerve injuries. However, the materials selected for use in the repair of peripheral nerve injuries, in particular multiple injuries and large-gap defects, must be chosen carefully. Various methods and materials for protecting the healthy tissue and repairing peripheral nerve injuries have been described, and each method or material has advantages and disadvantages. Recently, a large amount of research has been focused on tissue-engineered materials for the repair of peripheral nerve injuries. Using the keywords "peripheral nerve injury", "autotransplant", "nerve graft", and "biomaterial", we retrieved publications using tissue-engineered materials for the repair of peripheral nerve injuries appearing in the Web of Science from 2010 to 2014. The country with the most total publications was the USA. The institutions that were the most productive in this field include Hannover Medical School (Germany), Washington University (USA), and Nantong University (China). The total number of publications using tissue-engineered materials for the repair of peripheral nerve injuries gradually increased over time, as did the number of Chinese publications, suggesting that China has made many scientific contributions to this field of research.

Key Words: *nerve regeneration; peripheral nerve; nerve autograft; nerve transplantation; biomaterial; tissue engineering; neural regeneration*

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Introduction
Peripheral nerve injuries can cause severe sensory loss or secondary injuries to the peripheral nerve tissues, making them one of the most pressing problems in the fields of traumatic surgery and microsurgery. Satisfactory treatments for these problems are lacking. After a peripheral nerve injury occurs, the injection of nerve growth factors can promote nerve regeneration. However, this approach is ineffective for large-gap peripheral nerve defects, making nerve transplants necessary for the timely repair of such peripheral nerve injuries (Lundborg et al., 1997; Matsumoto et al., 2000). Tissue engineering methods provide new techniques for the repair of peripheral nerve injuries because tissue-engineered materials can reduce the risk of fibrosis and desmoplasia, promote and guide axon growth, and bridge nerve defects after peripheral nerve injury (Heath et al., 1998; Kim et al., 2008). Among the various methods for the repair of peripheral nerve injuries, the research and clinical application of nerve autografts and tissue-engineered materials has been increasing. Nerve autografts are considered the gold standard for the repair of peripheral nerve injuries in the clinic because they pose little risk of immunological rejection (Rinker et al., 2014). However, their clinical application is restricted by the limited tissue supply. In contrast, tissue-engineered materials can be made from a wide range of sources. In the present study, we used bibliometric analysis methods to determine the advantages and disadvantages of nerve autografts and tissue-engineered materials for the repair of peripheral nerve injuries.

Data and Methodology
We searched the Web of Science database provided by Thomson Reuters for publications in English regarding nerve autografts and tissue-engineered materials for the repair of peripheral nerve injuries from January 2010 to December 2014 using the key words "peripheral nerve injury", "autotransplant", "nerve graft", and "biomaterial". A total of 1,036 publications on nerve autografts and 472 publications on tissue-engineered materials were retrieved.

The inclusion criteria were publications on: (1) nerve allografts for the repair of peripheral nerve injuries; (2) nerve autografts for the repair of peripheral nerve injuries; (3) tissue-engineered materials for the repair of peripheral nerve injuries; and (4) topics closely associated with nerve autografts or tissue-engineered materials.

The exclusion criteria were repeated studies and meta-analysis papers.

Using the SCI database and Excel software, the extracted records were statistically analyzed for their country of origin, research area, institution, publication year, type of publication (including original research articles, reviews, meeting abstracts, proceedings papers, book chapters, and editorial material), and publication journal.

Results

Therapeutic effects of different graft materials for the repair of peripheral nerve injuries

Nerve transplants used for the repair of peripheral nerve injuries include nerve autografts, nerve allografts, and tissue-engineered materials (Bădoiu et al., 2014). These different grafts have their own advantages and disadvantages (**Table 1**).

Nerve autografts are generally isolated from autologous tissues, such as small nerves, vessels, and muscle. Replacing injured peripheral nerves with nerve autografts is currently considered the gold standard for the repair of peripheral nerve injuries because they minimize immunological reactions and provide a suitable microenvironment for nerve regeneration, which promotes a therapeutic effect (Radtke et al., 2014). Still, nerve autografts have many limitations. For example, although vein has some advantages for the repair of peripheral nerve injuries including inertia, degradation resistance, and a low cost, the donor-site complications should be considered (Tom et al., 2011; Leuzzi et al., 2014). Free fat is an abundant source material, but its therapeutic effects on the repair of peripheral nerve injuries remains uncertain. In addition, the kinetics of fat tissue reabsorption are not clearly defined. Gastrocolic omentum can also be used to repair large areas of injured peripheral nerve because it contains neurotrophic factors and pro-angiogenic factors. However, the main disadvantage of this method is that the gastrocolic omentum flap must be harvested through a laparoscopic operation, which increases the risk of injury (Hernández-Cortés et al., 2014; Sivak et al., 2014). To address these problems, research has focused on nerve autografts and tissue-engineered materials for the repair of peripheral nerve injuries.

Bibliometric analysis of publications on nerve autografts for the repair of peripheral nerve injuries from 2010 to 2014 indexed in the Web of Science

Distribution of publications by year

The total number of publications on nerve autografts for the repair of peripheral nerve injuries from 2010 to 2014 indexed in the Web of Science showed a slight, but not significant, increase over time. A total of 1,036 publications were retrieved, including 180 in 2010, 229 in 2011, 200 in 2012, 203 in 2013, and 224 in 2014, indicating that 2011 was the most productive year (**Figure 1**).

Distribution of publications by country

The countries that published articles on nerve autografts for the repair of peripheral nerve injuries from 2010 to 2014 in the Web of Science are shown in **Table 2**.

A total of 1,036 publications on nerve autografts for the repair of peripheral nerve injuries from 2010 to 2014 were retrieved from the Web of Science. The country with the largest total number of publications on this topic was the USA (n = 304, 29.344%), followed by China (n = 219), Germany (n = 90), Japan (n = 76), Italy (n = 52), Iran (n =48), England (n = 48), Canada (n = 43), South Korea (n = 37), then Sweden (n = 34). Three Asian countries are included among the top countries publishing articles on this topic, suggesting that these Asian countries have made significant contributions to the use of nerve autografts for the repair of peripheral nerve injuries.

Distribution of publications by institution

Among the top 10 institutions publishing articles on nerve autografts for the repair of peripheral nerve injuries from 2010 to 2014 indexed in the Web of Science, the institution producing the most publications was Hannover Medical School (Germany) with 29 publications (2.799%), followed by the University of Washington (USA; n = 26), Urmia University (Iran; n = 21), Nantong University (China; n = 21), University of Saskatchewan (Canada; n = 20), University of Manchester (England; n = 20), Islamic Azad University (Iran; n = 19), Miami University (USA; n = 18), University of Turin (Italy; n = 17), then Umea University (Sweden; n = 17). Nantong University in China was ranked fourth (**Figure 2**).

Distribution of publications by article type

Among the 1,036 publications on nerve autografts for the repair of peripheral nerve injuries from 2010 to 2014 indexed in the Web of Science, 882 (85.135%) were original research articles, 119 (11.486%) were reviews, 30 were meeting abstracts, 10 were editorial materials, and the remaining were other types. The original research articles clearly outnumbered the other publication types (**Table 3**).

Distribution of publications by funding agency

The distribution of publications on nerve autografts for the repair of peripheral nerve injuries from 2010 to 2014 indexed in the Web of Science by funding agency is shown in **Table 4**.

Among the funding agencies that supported the research on nerve autografts for the repair of peripheral nerve injuries published from 2010 to 2014 and retrieved from the Web of Science, the largest number of publications was from the National Natural Science Foundation of China (n = 78, 7.529%), followed by National Institutes of Health (n = 59, 6.795%), High-Tech Research and Development Program of China (863 Program) (n = 15, 1.448%), then other agencies ($n < 10$).

Bibliometric analysis of publications on tissue-engineered materials for the repair of peripheral nerve injuries from 2010 to 2014 indexed in the Web of Science

Despite the rapid development of tissue-engineered materials for the repair of peripheral nerve injuries, none of the investigated scaffold materials have performed better than nerve autografts. Scaffolds constructed from acellular nerve matrix or artificially synthesized degradable materials can be used to repair peripheral nerve injuries, but the addition of seed cells and neurotrophic factors is necessary to promote nerve regeneration (Beigi et al., 2014; Pateman et al., 2015). Assessment of the functional recovery of innervated muscles after the repair of peripheral nerve injuries is increasingly important. Therefore, there is an urgent need to determine the best

Table 1 Advantages and disadvantages of nerve grafts for the repair of peripheral nerve injury

Nerve transplant	Advantages	Disadvantages
Nerve autograft	-Simple, easy, and safe to obtain -Easy to suture to the injured tissue -No risk of immunological rejection -Provides a suitable environment for nerve regeneration	-Limited amount of tissue -Donor site morbidity and potential loss of function -Limited number of grafts
Nerve allograft	-Unlimited source tissue -No donor site trauma for the recipient	-Lack of appropriate animal donor tissue -Uncertain histocompatibility -Ethical and legal concerns
Tissue-engineered material	-Fabricated from polymers or biomacromolecules -Easy to produce -Unlimited source materials -No donor site trauma	-Antigenicity -Degradable biomaterials are expensive -Exhibit poor tenacity, making them difficult to suture to the injured nerve

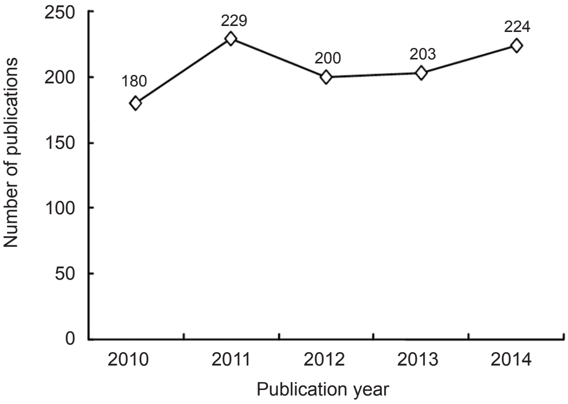

Figure 1 Number of publications on nerve autograft for the repair of peripheral nerve injuries from 2010 to 2014 in the Web of Science.

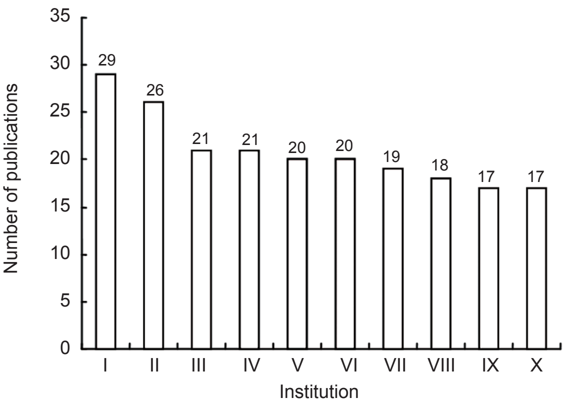

Figure 2 The top 10 institutions publishing articles on nerve autografts for the repair of peripheral nerve injuries from 2010 to 2014 indexed in the Web of Science.
I: Hannover Medical School; II: University of Washington; III: Urmia University; IV: Nantong University; V: University of Saskatchewan; VI: University of Manchester; VII: Islamic Azad University; VIII: Miami University; IX: University of Turin; X: Umea University.

repair material and graft construction protocol for achieving morphological and structural repair and functional recovery of injured peripheral nerves (Koudehi et al., 2014). The biomaterials often used for tissue engineering applications include artificially synthesized materials and modified natural materials, and they can be classified as either degradable or non-degradable. Ideal tissue-engineered materials should be histocompatible, non-toxic, promote cellular activity, and facilitate cell adhesion and growth (Ramburrun et al., 2014).

Table 2 Top ten countries that published articles on nerve autografts for the repair of peripheral nerve injuries from 2010 to 2014 in the Web of Science

Country	No. of articles	Proportion (%)
USA	304	29.344
China	219	21.139
Germany	90	8.687
Japan	76	7.336
Italy	52	5.019
Iran	48	4.633
England	48	4.633
Canada	43	4.151
South Korea	37	3.571
Sweden	34	3.282

Table 3 Types of publications on nerve autograft for the repair of peripheral nerve injuries from 2010 to 2014 indexed in the Web of Science

Type of publication	No. of publications	Proportion (%)
Original research Article	882	85.135
Reviews	119	11.486
Proceedings paper	30	2.896
Editorial material	10	0.965
Book chapter	7	0.676
Meeting abstract	5	0.483
Letter	3	0.290
News item	1	0.097

Note: Proceedings papers were often retrieved from the Web of Science as original research articles and were included in both categories here. Therefore, the total number of publications summed over all categories is larger than the total number of articles retrieved from the Web of Science.

Distribution of publications by year

The total number of publications on tissue-engineered materials for the repair of peripheral nerve injuries from 2010 to 2014 indexed in the Web of Science significantly increased over time. A total of 472 publications were retrieved, including 68 (14.407) in 2010, 75 (15.89%) in 2011, 86 (18.22%) in 2012, 110 (23.305%) in 2013, and 133 (28.178%) in 2014 (**Figure 3**).

Distribution of publications by number of citations

Bibliometrics, first proposed by Alan Pritchard in 1969, uses quantitative and statistical methods, based on the classification

Table 5 The most cited publications on tissue-engineered materials for the repair of peripheral nerve injuries from 2010 to 2014 indexed in the Web of Science

Title	Author	Journal	Year of publication	Total citations	Frequency
Current applications and future perspectives of artificial nerve conduits	Jiang X, et al.	*Experimental Neurology*	2010	119	19.83
Adipose-derived stem cells enhance peripheral nerve regeneration	di Summa PG, et al.	*Journal of Plastic Reconstructive and Aesthetic Surgery*	2010	90	15.00
Electrospun nanofibers for regenerative medicine	Liu WY, et al.	*Advanced Healthcare Materials*	2012	84	21.00
Randomized trial of percutaneous tibial nerve stimulation versus sham efficacy in the treatment of overactive bladder syndrome: results from the SUmiT trial	Peters KM, et al.	*Journal of Urology*	2010	75	12.50
FDA approved guidance conduits and wraps for peripheral nerve injury: A review of materials and efficacy	Kehoe S, et al.	*Injury*	2012	68	17.00
Silk fibroin biomaterials for tissue regenerations	Kundu B, et al.	*Advanced Drug Delivery Reviews*	2013	66	22.00

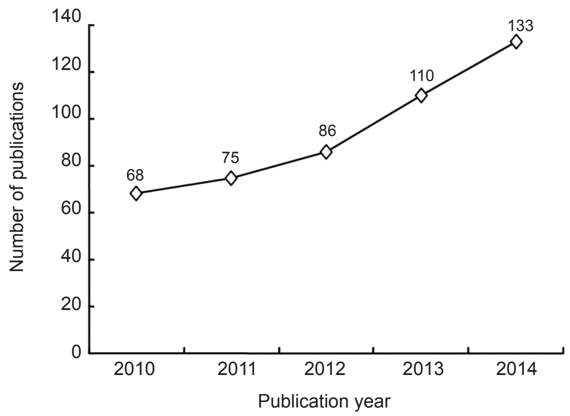

Figure 3 Number of publications on tissue-engineered materials for the repair of peripheral nerve injuries from 2010 to 2014 indexed in the Web of Science.

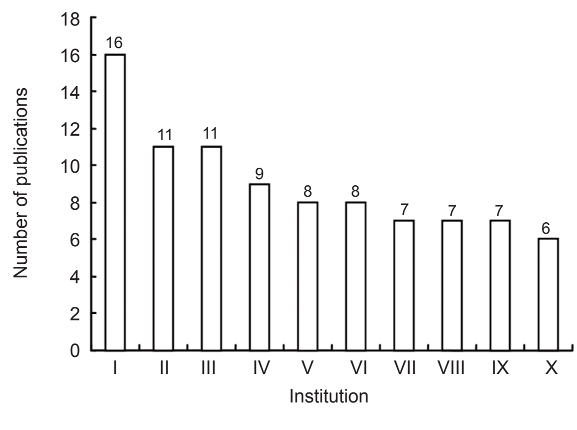

Figure 4 Top 10 institutions publishing the largest number of articles on tissue-engineered materials for the repair of peripheral nerve injuries from 2010 to 2014 indexed in the Web of Science.
I: Nantong University; II: University of Michigan; III: University College London; IV: University of Turin; V: Hannover Medical School; VI: Chinese Academy of Sciences; VII: Washington University; VIII: Tufts University; IX: Mayo Clinic; X: University of Milan.

Table 4 The distribution of publications on nerve autografts for the repair of peripheral injuries from 2010 to 2014 indexed in the Web of Science by funding agency

Funding agency	No. of publications	Proportion (%)
National Natural Science Foundation of China	78	7.529
National Institutes of Health	59	6.795
Hi Tech Research and Development Program of China 863 Program	15	1.448
Priority Academic Program Development of Jiangsu Higher Education Institutions PAPD	8	0.772
German Research Foundation	8	0.772
State of Florida	7	0.676
European Union	7	0.676
Department of Defense	7	0.676
Swedish Medical Research Council	6	0.579

Table 6 Top ten countries that published articles on tissue-engineered materials for the repair of peripheral nerve injuries indexed in the Web of Science from 2010 to 2014

Country	Number of publications	Proportion (%)
USA	145	30.720
China	72	15.254
Italy	44	9.322
Germany	38	8.051
England	36	7.627
Japan	31	6.568
France	24	5.085
Canada	18	3.814
South Korea	16	3.390
Spain	15	3.178

Table 7 The distribution of publications on tissue-engineered materials for the repair of peripheral injuries from 2010 through 2014 indexed in the Web of Science by funding agency

Funding agency	Number of publications	Proportion (%)
National Natural Science Foundation of China	38	8.051
National Institutes of Health	35	7.416
Wellcome Trust	7	1.483
US Army	5	1.059
Priority Academic Program Development of Jiangsu Higher Education Institutions PAPD	5	1.059
NSF	5	1.059
HI Tech Research and Development Program of China 863 Program	5	1.059
European Union	5	1.059

Table 8 The journals that have published the most articles on tissue-engineered materials for the repair of peripheral nerve injuries indexed in the Web of Science

Journal	Number of publications	Proportion (%)
Biomaterials	28	5.932
PLoS One	24	5.085
Journal of Biomedical Materials Research Part A	14	2.966
Tissue Engineering Part A	7	1.483
Neural Regeneration Research	6	1.271
Journal of Neural Engineering	5	1.059
Biomed Research International	5	1.059
Neuroscience Letters	4	0.847

of publications by individual features, to describe, evaluate, and predict the current status and developing trends in scientific techniques. Citation number has recently been considered a standard for classifying "classical publications". According to bibliometrics, a major criterion for measuring the quality of a publication is the number of citations, which is an important index for how peer reviewers evaluate the academic quality of an article. Higher citation rates indicate that an article has had a greater impact on subsequent research (Yue et al., 2008). The publications on tissue-engineered materials for the repair of peripheral nerve injuries indexed in the Web of Science from 2010 to 2014 with the most citations are shown in **Table 5**.

Distribution of publications by country

The countries that published articles on tissue-engineered materials for the repair of peripheral nerve injuries from 2010 to 2014 indexed in the Web of Science are shown in **Table 6.**

A total of 472 publications on tissue-engineered materials for the repair of peripheral nerve injuries from 2010 to 2014 were retrieved from the Web of Science. The country with the largest total number of publications on this topic was the USA (n = 145, 30.72%), followed by China (n = 72), Italy (n = 44), Germany (n = 38), England (n = 36), Japan (n = 31), then other countries (n < 30). Three Asian countries are listed among the top countries publishing articles on this topic, suggesting that these Asian countries have made significant contributions to the use of tissue-engineered materials for the repair of peripheral nerve injuries.

Distribution of publications by institution

The top 10 institutions publishing the largest number of articles on tissue-engineered materials for the repair of peripheral nerve injuries from 2010 to 2014 indexed in the Web of Science are shown in **Figure 4**.

Among the top 10 institutions publishing the largest number of articles on tissue-engineered materials for the repair of peripheral nerve injuries from 2010 to 2014 indexed in the Web of Science, the institution that published the largest number was Nantong University (China) with 16 publications (3.39%), followed by the University of Michigan (USA; n = 11), University College London (England; n = 11), University of Turin (Italy; n = 9), Hannover Medical School (Germany; n = 8), Chinese Academy of Sciences (China; n = 8), Washington University (USA: n = 7), Tufts University (USA; n = 7), Mayo Clinic (USA; n = 7), and University of Milan (Italy; n = 6). Nantong University and the Chinese Academy of Sciences were within the top 10 institutions publishing articles on this topic.

Distribution of publications by funding agency

The distribution of publications on tissue-engineered materials for the repair of peripheral nerve injuries from 2010 to 2014 indexed in the Web of Science by funding agency is shown in **Table 7**.

Among the funding agencies that supported publications on tissue-engineered materials for the repair of peripheral nerve injuries from 2010 to 2014 retrieved from the Web of Science, the funding agency that supported the largest number of publications was the National Natural Science Foundation of China (n = 38, 8.051%), followed by the National Institutes of Health (n = 35, 7.416%), and then other agencies (n < 10). China has financially supported more published studies on tissue-engineered materials for the repair of peripheral nerve injuries than any other country.

Distribution of publications by journal

Among the journals publishing articles on tissue-engineered materials for the repair of peripheral nerve injuries from 2010 to 2014 retrieved from the Web of Science, the journal with the largest number of articles was *Biomaterials* with 28 publications (5.932%), followed by *PLoS One* (n = 24), the *Journal of Biomedical Materials Research Part A* (n = 14), *Tissue engineering Part A* (n = 7), *Neural Regeneration Research* (n = 6), *Journal of Neural Engineering* (n = 5), *Biomed Research International* (n = 5), and *Neuroscience Letters* (n = 4). These results will help scholars in this research field know which journals publish work on tissue-engineered materials for the repair of peripheral nerve injuries, increasing publication success rate and better disseminating the research findings. The journals that have published the largest number of articles on tissue-engineered materials for the repair of peripheral nerve injuries from 2010 to 2014 retrieved from the Web of Science are shown in **Table 8**.

Discussion

The repair process for peripheral nerve injuries is complex, and functional recovery of the injured peripheral nerve can be inhibited by many factors, including the slow speed of nerve regeneration, limited availability of nerve autografts, and immunological rejection caused by nerve allografts (Alluin et al., 2006; Campbell, 2008). Interest and research in the use of tissue-engineered materials as nerve grafts has been increasing in the field of peripheral nerve injury repair, with a large number of articles published on this topic (Nagao et al., 2011). Over the last 5 years, the number of publications concerning different materials, in particular tissue-engineered materials, used for the repair of peripheral nerve injuries has tended to increase. Among the studies on this topic indexed in the Web of Science, the USA published the largest number of articles on tissue-engineered materials for the repair of peripheral nerve injuries, suggesting that it significantly contributes to research in this field. China produced the second most publications, and the number of publications from China increased each year. Hannover Medical School (Germany), Washington University (USA), and Nantong University (China) were the institutions that produced the largest number of publications on tissue-engineered materials for the repair of peripheral nerve injuries. These results point out the core institutions that have published articles on tissue-engineered materials for the repair of peripheral nerve injuries, which will help scientists to develop technical communications and research collaborations. The funding agencies that supported the largest number of publications on tissue-engineered materials for the repair of peripheral nerve injuries are the National Natural Science Foundation of China and the National Institutes of Health. China has made many significant contributions to research on tissue-engineered materials for the repair of peripheral nerve injuries.

The treatment of peripheral nerve injuries is a difficult medical problem. With the rapid development of science and technology, and tissue engineering in particular, the development of a graft to treat peripheral nerve injuries is promising (Chang, 2009). Such a tissue-engineered material graft will have good biocompatibility and degradation properties, making it the preferred nerve graft for the repair of peripheral nerve injuries (Mukhatyar et al., 2014; Rochkind, et al., 2014).

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